

I U C L I D

Data Set

Existing Chemical : ID: 84-66-2
CAS No. : 84-66-2
EINECS Name : diethyl phthalate
EC No. : 201-550-6
TSCA Name : 1,2-Benzenedicarboxylic acid, diethyl ester
Molecular Formula : C12H14O4

Producer related part
Company : ExxonMobil Biomedical Sciences Inc.
Creation date : 16.10.2000

Substance related part
Company : ExxonMobil Biomedical Sciences Inc.
Creation date : 16.10.2000

Status :
Memo : ACC Phthalate Ester Panel HPV Testing Group

Printing date : 13.12.2006
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Number of pages : 35

Chapter (profile) : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4
Flags (profile) : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE),
Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1. General Information

Id 84-66-2
Date 13.12.2006

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : lead organisation
Name : ACC Phthalate Esters Panel HPV Testing Group
Contact person : Dr. Marian Stanley
Date :
Street : 1300 Wilson Blvd.
Town : 22209 Arlington, VA
Country : United States
Phone : (703) 741-5623
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Cedex :
Email :
Homepage :

Remark : The American Chemistry Council Phthalate Esters Panel includes the following member companies:

BASF Corporation
CONDEA Vista Company
Eastman Chemical Company
ExxonMobil Chemical Company
Ferro Corporation
ICI Americas / Uniqema
Sunoco Chemicals
Teknor Apex Company

02.11.2001

20.10.2000

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

Comment : This chemical is part of the Low Molecular Weight Phthalate Esters subcategory. The subcategory includes the following two CAS numbers: 131-11-3 and 84-66-2

Remark : This chemical is part of the Low Molecular Weight Phthalate Esters subcategory. The subcategory includes the following two CAS numbers and names:
131-11-3 1,2-Benzenedicarboxylic acid, dimethyl ester (DMP)
84-66-2 1,2-Benzenedicarboxylic acid, diethyl ester (DEP)

The phthalate esters comprise a family of chemicals synthesized by esterifying phthalic anhydride with various alcohols in the presence of an acid catalyst. Phthalate esters are all 1,2-benzenedicarboxylic acids with side chain ester groups ranging from C1 to approximately C13. The structural characteristics of the ester side chains affect both the physical/chemical and biological properties of phthalate esters.

Phthalate esters are generally clear to yellow, oily liquids with high boiling ranges (>250°C) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils. The aqueous solubility of phthalate esters is inversely related to their molecular weights. Lower molecular weight phthalates exhibit slight to moderate water solubility, whereas, higher molecular weight phthalates exhibit very low solubility.

The phthalate esters were subdivided into three subcategories based on their physicochemical and toxicological properties. The phthalate esters in this subcategory, Low molecular weight phthalates, are produced from alcohols with straight-chain carbon backbones of <C3. The U.S. HPV chemicals, dimethyl (DMP) and diethyl (DEP) phthalate, are included in this subcategory. Low molecular weight phthalates are commonly used as solvents or in cellulose acetate polymers rather than as plasticizers for PVC. Their relatively higher volatility and water solubility give them properties different than other phthalate esters in this category, some of which translate to different biological properties. In particular, these phthalates have greater aqueous solubility, resulting in a potential to cause acute toxic effects in aquatic organisms.

14.04.2006

1.1.0 SUBSTANCE IDENTIFICATION**1.1.1 GENERAL SUBSTANCE INFORMATION**

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	
Colour	:	
Odour	:	

02.11.2001

1.1.2 SPECTRA**1.2 SYNONYMS AND TRADENAMES****1.3 IMPURITIES****1.4 ADDITIVES****1.5 TOTAL QUANTITY****1.6.1 LABELLING**

1.6.2 CLASSIFICATION**1.6.3 PACKAGING****1.7 USE PATTERN**

Type of use : industrial
Category : Basic industry: basic chemicals

Remark : Low molecular weight phthalates are commonly used as solvents or in cellulose acetate polymers rather than as plasticizers for PVC.

02.11.2001

1.7.1 DETAILED USE PATTERN**1.7.2 METHODS OF MANUFACTURE****1.8 REGULATORY MEASURES****1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES****1.8.2 ACCEPTABLE RESIDUES LEVELS****1.8.3 WATER POLLUTION****1.8.4 MAJOR ACCIDENT HAZARDS****1.8.5 AIR POLLUTION****1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES****1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS****1.9.2 COMPONENTS****1.10 SOURCE OF EXPOSURE**

1. General Information

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1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2. Physico-Chemical Data

Id 84-66-2
Date 13.12.2006

2.1 MELTING POINT

Value : -40 °C
Sublimation :
Method : other: no data
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Remark : Data are from a peer reviewed literature review of data from a variety of sources including manufacturer's data or handbook values.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary is assigned a reliability of 2 because there is limited information on how the data were developed.
Flag : Critical study for SIDS endpoint
31.03.2006 (14)

Value : -1.7 °C
Sublimation : no
Method : other: calculation
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method : Melting point calculation by MPBPWIN ver. 1.41 using calculation methods of Joback and Gold and Ogle.
Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation. However, the melting point calculation in EPI Suite™ gives erroneously high results for the phthalate esters.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (3) invalid
05.07.2006 (6)

2.2 BOILING POINT

Value : 282 °C at 1013 hPa
Decomposition :
Method : other
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method : Boiling point calculation by MPBPWIN ver. 1.41 using calculation method of Stein and Brown.
Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint
31.03.2006 (6)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : .000648 hPa at 25 °C
Decomposition : no
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.
Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for vapour pressure, represent the definitive and currently accepted physicochemical database for selected phthalate esters including diethyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume ($\text{cm}^3 \text{mol}^{-1}$). The Le Bas molar volume used for diethyl phthalate ester was $254.0 \text{ cm}^3 \text{mol}^{-1}$.

$\text{Log CS(WL)} = -0.012V + 5.8$, $n = 35$ (solubility in water)
 $r^2 = 0.98$, $\text{SE} = 0.39$

$\text{Log CS(AL)} = -0.013V - 1.3$, $n = 15$ (solubility in air)
 $r^2 = 0.87$, $\text{SE} = 0.33$

$\text{Log CS(OL)} = -0.016V + 3.4$, $n = 68$ (solubility in octanol)
 $r^2 = 0.19$, $\text{SE} = 0.41$

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
 The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.
Flag : Critical study for SIDS endpoint

31.03.2006

(2)

Value : .0034 hPa at 25 °C
Decomposition : no
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Vapor pressure calculation by MPBPWIN ver. 1.41 using calculation method of Grain.

Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.

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Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

14.04.2006

(6)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : 2.54 at 25 °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.

Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for partition coefficient, represent the definitive and currently accepted physicochemical database for selected phthalate esters including diethyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm³ mol⁻¹). The Le Bas molar volume used for diethyl phthalate ester was 254.0 cm³ mol⁻¹.

Log CS(WL) = -0.012V + 5.8, n = 35 (solubility in water)
r² = 0.98, SE = 0.39

Log CS(AL) = -0.013V - 1.3, n = 15 (solubility in air)
r² = 0.87, SE = 0.33

Log CS(OL) = -0.016V + 3.4, n = 68 (solubility in octanol)
r² = 0.19, SE = 0.41

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions

The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

31.03.2006

(2)

Partition coefficient : octanol-water
Log pow : 2.65 at 25 °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

2. Physico-Chemical Data

Id 84-66-2

Date 13.12.2006

Method : Partition coefficient by LOGKOWWIN ver. 1.67 using an atom/fragment calculation method of Meylan and Howard.
Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

31.03.2006

(6)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : 591 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: calculated
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.

Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for water solubility, represent the definitive and currently accepted physicochemical database for selected phthalate esters including diethyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm³ mol⁻¹). The Le Bas molar volume used for diethyl phthalate ester was 254.0 cm³ mol⁻¹.

$\text{Log CS(WL)} = -0.012V + 5.8$, n = 35 (solubility in water)
r² = 0.98, SE = 0.39

$\text{Log CS(AL)} = -0.013V - 1.3$, n = 15 (solubility in air)
r² = 0.87, SE = 0.33

$\text{Log CS(OL)} = -0.016V + 3.4$, n = 68 (solubility in octanol)
r² = 0.19, SE = 0.41

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
The value was calculated based on the QSPR (quantitative structure-

2. Physico-Chemical Data

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Date 13.12.2006

property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint
03.04.2006 (2)

Solubility in : Water
Value : 287.2 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: calculated
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Water solubility calculated using WSKOWN ver 1.41 based on Kow correlation method of Meylan and Howard. Kow used in calculation was 2.42.

Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.

Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

03.04.2006 (6)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3. Environmental Fate and Pathways

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3.1.1 PHOTODEGRADATION

Type : air
Light source : Sun light
Light spectrum : nm
Relative intensity : 1 based on intensity of sunlight
INDIRECT PHOTOLYSIS
Sensitizer : OH
Conc. of sensitizer : 1500000 molecule/cm³
Rate constant : .000000000003466 cm³/(molecule*sec)
Degradation : 50 % after 37 hour(s)
Deg. product : not measured
Method :
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Photodegradation rate calculated by AOPWIN ver. 1.91 based on the methods of Atkinson.
Remark : 50% degradation after 37.03 hrs or 3.09 days based on a 12-hour day. The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPI SuiteTM, 2000) calculates a chemical half-life for a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated), based on an OH- reaction rate constant and a defined OH- concentration.

EPI SuiteTM is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint
05.12.2006 (6)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : 2.9 year at 25 °C
t1/2 pH9 : at °C
Deg. product :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on work for EPA by T. Mill et al.
Remark : EPI SuiteTM is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.
Flag : Critical study for SIDS endpoint

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3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : other: air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
-----------	----------------

Molecular Weight	222.24
Temperature	25° C
Log Kow	2.54
Water Solubility	591 g/m3
Vapor Pressure	0.0648 Pa
Melting Point	-40°C

Result : Using the Mackay Level I calculation, the following distribution is predicted for 1,2-Benzenedicarboxylic acid, diethyl ester:

% Distribution	Compartment
0.4	Air
75.8	Water
23.3	Soil
0.5	Sediment
0.0	Suspended Sediment
0.0	Biota

Test substance : CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

Flag : Critical study for SIDS endpoint

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Media : other: air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
-----------	----------------

Molecular Weight	222.24
Temperature	25° C
Log Kow	2.54

3. Environmental Fate and Pathways

Id 84-66-2
Date 13.12.2006

Water Solubility 591 g/m3
Vapor Pressure 0.0648 Pa
Melting Point -40°C

Emissions rates used in the calculation:

Compartment Rate (kg/hr)

Air 1000
Water 1000
Soil 1000

Half-lives used in the calculation:

Compartment Half-life (hr)

Air 74.06a
Water 120b
Soil 420c
Sediment 420c

a - as calculated using AOPWIN version 1.91, a subroutine of the computer program EPI Suite™ version 3.12 and normalized to a 24 hour day [Environmental Protection Agency (EPA) (2000). EPI Suite™, Estimation Program Interface Suite, v3.12. U.S. EPA, Washington, DC, USA.]

b - based on biodegradation data from Sugatt, R.H. et al, 1983 Shake Flask Biodegradation of 14 Commercial Phthalate Esters. Syracuse Research Corporation, Syracuse, NY. SRC# L1543-05. Performed for Chemical Manufacturers Association.

Boethling R (2000). HPVC-Screening Tool: Using Ready and Inherent Biodegradability Data to Derive Input Data for the EQC Model, Appendix 10 in Environment Canada, Environmental Categorization for Persistence Bioaccumulation and Inherent Toxicity of Substances on the Domestic Substance List Using QSARs, Results of an international workshop hosted by Chemicals Evaluation Division of Environment Canada, Nov. 11-12, 1999, in Philadelphia, PA, USA.

c - based on Boethling, R. recommendation that half-lives of 3 to 4 times longer than surface water should be used for soil and sediment.

Result

: Using the Mackay Level III calculation, the following distribution is predicted for 1,2-Benzenedicarboxylic acid, diethyl ester:

Compartment % Distribution
Air 3.4
Water 16.9
Soil 79.7
Sediment 0.0

Test substance Reliability

: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
: (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

Flag
11.05.2006

: Critical study for SIDS endpoint

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3.4 MODE OF DEGRADATION IN ACTUAL USE

3. Environmental Fate and Pathways

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Date 13.12.2006

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: Adapted domestic sewage and soil
Concentration : 20 mg/l related to
related to
Contact time : 28 day(s)
Degradation : = 94.6 (±) % after
Result :
Deg. product :
Method : other
Year :
GLP : yes
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Method/Guideline - USEPA 1982, CO2 Evolution, Shake Flask (modified Gledhill).
Inoculum - Domestic sewage and soil.
Kinetics - Not Reported
Degradation Products - Not Reported
Analytical Monitoring - Yes
Result : Concentration - Nominal test concentration = 20 mg/L for test substance and glucose.

Units - % biodegradation

Result - >99% primary biodegradation and 94.6% (s.d. +/-2.3%) ultimate biodegradation.

Primary degradation is expressed as the loss of test substance based on analytical measurements of parent test substance. Ultimate biodegradation is expressed as the percentage of ThCO2 (based on test substance) evolved in each flask.

Test condition : Test Conditions - Inoculum was aged for 2 weeks prior to test initiation. The test chemical was added to flasks containing medium and inoculum. The flask were incubated and shaken in the dark for 28 days. Three replicates for CO2 evaluation and 4 replicates for primary degradation were tested. The CO2 production was captured in barium hydroxide solution. Primary biodegradation was determined at the beginning, middle and end by GC FID of entire contents of one replicate. A glucose and blank were also tested. 2L Erlenmeyer flasks were used as test vessels. The pH at initiation was 7.0 to 7.2. Test flasks were shaken at a rate of 120 rpm at 22 +/- 2 deg C.

Test substance : Diethyl phthalate (DEP CAS# 84-66-2)
(1,2,-benzenedicarboxylic acid, diethyl ester)
Synonym: DEP
No information on purity, but DEP was analytically confirmed to be within commercial specifications.

Conclusion : The substance can biodegrad to a high extent using an acclimated population of microorganisms obtained from a sewage treatment system and soil.

Reliability : (1) valid without restriction
This summary is rated a "1" because it followed a USEPA standard guideline, which describes a procedure specifically designed to evaluate biodegradation under acclimated conditions, and the results were reviewed for reliability and assessed as valid.

Flag : Critical study for SIDS endpoint
26.04.2006

(16) (17)

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3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: flow through												
Species	: <i>Salmo gairdneri</i> (Fish, estuary, fresh water)												
Exposure period	: 120 hour(s)												
Unit	: mg/l												
LC50	: = 12 measured/nominal												
Limit test	:												
Analytical monitoring	: yes												
Method	: other												
Year	: 1975												
GLP	: yes												
Test substance	: other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester												
Method	: Method/Guideline - U.S. EPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. 1975.												
Result	<p>Statistical methods - Moving average angle, Probit or Bionomial Concentration.</p> <p>: 96 hr LC50 = 12.0 mg/L (95% CI = 10.0 to 15.0 mg/L) Mean measured values were used in the LC50 calculation.</p> <p>Nominal test concentrations: control, 2.5, 5.0, 10.0, 20.0, and 40.0 mg/L. Mean measured test concentrations: <0.0067, 1.9, 3.8, 8.4, 16.0, and 33.0 mg/L.</p> <p>Analytical samples were taken at time zero and on a composite of replicates at study termination. Measured values dropped slightly during the exposure period.</p> <p>% Mortality results at 96 hrs per replicate for control and treatment levels: Conc. (mg/L) Rep1/Rep2</p> <table> <tr><td>Control</td><td>0 / 0</td></tr> <tr><td>1.9</td><td>0 / 0</td></tr> <tr><td>3.8</td><td>0 / 0</td></tr> <tr><td>8.4</td><td>20 / 15</td></tr> <tr><td>16.0</td><td>70 / 75</td></tr> <tr><td>33.0</td><td>100 / 100</td></tr> </table> <p>Test condition</p> <p>: Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham Mass. town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter. The diluter delivered a series of stock dilutions to the test vessels. Test chambers were glass tanks containing 15L of solution. The diluter maintained a water turnover rate of 5 to 8 tank volumes per day. Two replicates of ten organisms were tested per treatment and control. Analytical method was Gas Liquid Chromatography (GLC) with electron capture detection.</p> <p>Fish mean length = 45 mm and mean wet weight = 0.76 g. Test temperature = 12 +/- 1 Deg C. The pH ranged from 7.1 to 7.4. The mean dissolved oxygen ranged from 8.6 to 9.5 mg/L. Ranges of total hardness and alkalinity as CaCO₃ of the dilution water were 20 to 26 mg/L and 14 to 22 mg/L, respectively.</p> <p>Test substance</p> <p>: Fish were obtained from a Montana supplier. Diethyl phthalate (CAS# 84-66-2) (1,2-benzenedicarboxylic acid, diethyl ester)</p>	Control	0 / 0	1.9	0 / 0	3.8	0 / 0	8.4	20 / 15	16.0	70 / 75	33.0	100 / 100
Control	0 / 0												
1.9	0 / 0												
3.8	0 / 0												
8.4	20 / 15												
16.0	70 / 75												
33.0	100 / 100												

Conclusion : Synonym: DEP
Purity: 100% active ingredient
: Test substance is toxic to fish below its water solubility level.
Data selected based upon routine species, measured data and representative value, as compared with those found in reference document, Staples et al. (1997).

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2006 (5) (15)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 86 measured/nominal
Analytical monitoring : yes
Method : other
Year : 1975
GLP : yes
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Method/Guideline - U.S. EPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians. 1975.

Result : Statistical methods - Moving average angle, Probit or Bionomial Concentration.
: 48 hr EC50 = 90.0 mg/L (95% CI = 77 to 100; based upon time zero analytical samples). Value was recalculated as 86.0 mg/L as per U.S. EPA current practices using mean of measured initiation and termination samples as reported in Staples et al. (1997).

Mean measured values were used in the final EC50 calculation.

Nominal test concentrations: control, 50, 86, 140, 240, and 400 mg/L.
Mean measured test concentrations of time 0 and 48 hr values: <0.007, 37.5, 69, 115, 195, and 335 mg/L.

Analytical samples taken at time zero and on a composite of replicates at termination. Measured values remained consistent during study exposure.

% Immobility results at 48 hrs per replicate for control and treatment levels:
Conc. (mg/L) Rep1/Rep2/Rep3

Control	0 / 0 / 0
37.5	0 / 0 / 0
69	0 / 20 / 40
115	100 / 80 / 80
195	100 / 100 / 100
335	100 / 100 / 100

Test condition : Test treatments were prepared by mixing the test substance and dilution water (fortified well water) in a Polytron homogenizer for 30 minutes. The stock solution was prepared at the highest treatment concentration. Dilutions of the stock were prepared for each treatment level. Three replicates of five organisms were tested per treatment. Test vessels were 250 ml beakers with 200 ml of test solution. Analytical method was Gas Liquid Chromatography (GLC).

Test temperature = 22 +/- 2 Deg C. The pH was 8.5 at initiation and

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Test substance : ranged from 8.2 to 8.3 on Day 2. Dissolved oxygen ranged from 7.9 to 8.3 at initiation and 7.9 to 8.4 on Day 2. Daphnia were <24 hours old and obtained from in-house stock.
: Diethyl phthalate (CAS# 84-66-2)
(1,2-benzenedicarboxylic acid, diethyl ester)
Synonym: DEP
Purity: unstated, but believed to be 100% active ingredient because the test material came from the same source as in the rainbow trout acute study.

Conclusion : Test substance is toxic to Daphnia below its water solubility level. Data selected based upon routine species, measured data and representative value, as compared with those found in reference document, Staples et al. (1997).

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
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4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint :
Exposure period : 8 day(s)
Unit : mg/l
EC50 : = 16 measured/nominal
Limit test :
Analytical monitoring : yes
Method : other
Year : 1978
GLP : yes
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Method/Guideline - EPA 600/9-78-018, Printz Algal Assay Bottle Test. 1978.
Statistical methods - Moving average angle, Probit or Bionomial
Test type - Static

Result : 192 hr (8 day) EC50 = 30.3 mg/L (95% CI = 21.6 to 38.3; based upon time zero analytical samples). Value was recalculated as 16 mg/L as per U.S. EPA current practices using mean of measured initiation and termination samples as reported in Staples et al. (1997).

Mean measured values were used in the final EC50 calculation.

Nominal test concentrations: control, 6.3, 12.5, 25.0, 50.0, and 100.0 mg/L.
Mean measured test concentrations of time 0 and 192 hr values: not detected, 3.65, 7.4, 15.2, 30.3, and 58.8 mg/L (detection limit was 0.1 mg/L).

Analytical samples taken at time zero and on a composite of replicates at termination. In-vivo chlorophyll a, measured until less than 5% change. Both cell number and in-vivo chlorophyll a, measured at termination. Control chlorophyll a or cell counts were not reported.

Chlorophyll a percent change relative to control on sampling days and cell number on day 8 results per treatment level:

Conc. Chlorophyll a percent change from control
(mg/L) Day 3 Day 5 Day 7 Day 8 Cell # Day 8

64.7	-52	-35	-10	-9	+4
133.0	-59	-41	-14	-14	-21
292.6	-71	-51	-48	-47	-47

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	597.7	-86	-84	-70	-71	-73
	1329.6	-95	-99	-99	-99	-99
Test condition	:	Test substance was added to Algal Growth Medium equal to the highest test concentration (1000 mg/L) and stirred for one hour and settled for one-half hour. Fifty percent (50%) dilutions were made of this stock solution using algal growth media (dilution water and control) and tested. Initial algal concentration was 2.0 E4 cells/ml. Replicate number was not cited.				
Test substance	:	Lighting = 4,030 lux, Test temperature = 24+/-1 Deg C. The pH was 7.6 at initiation and ranged from 7.9 to 8.9 on day 8. Algal culture stock was obtained from University of Texas at Austin, TX. Diethyl phthalate (CAS# 84-66-2) (1,2,-benzenedicarboxylic acid, diethyl ester) Synonym: DEP Purity: unstated, but believed to be 100% active ingredient as was provided in the rainbow trout study.				
Conclusion	:	Test substance is toxic to algae at or below its water solubility level. Data selected based upon routine species, measured data and representative value, as compared with those found in reference documnet, Staples et al. (1997).				
Reliability Flag	:	(2) valid with restrictions Critical study for SIDS endpoint				
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4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	other: reproduction rate and survival
Exposure period	:	21 day(s)
Unit	:	mg/l
NOEC	:	= 25
LOEC	:	= 59
Analytical monitoring	:	yes
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method	:	The test method followed a procedure developed at the testing lab, Springborn Laboratories, and generally followed the Daphnid chronic testing procedure described in OECD guideline 202 (1984).
Result	:	Five exposure concentrations were used in the study as follows with standard deviation in parenthesis: 130 (21); 59 (6); 25 (3); 16 (2); and 5.8 (1.4) Survival and reproduction was significantly different (p = 0.05) than the control in the two highest concentrations. LOEC = 59 mg/L NOEC = 25 mg/L MATC = 38.4 mg/L

mg/L	Po % Survival	Mean F1 Survival
------	------------------	---------------------

		Day 21	Day 21
	Control	90 (sd=9)	95 (sd=10)
	130	0 (sd=0)	No Survivors on day 21
	59	55 (sd=32)	0 (sd=0)
	25	86 (sd=5)	76 (sd=15)
	16	85 (sd=4)	88 (sd=15)
	5.8	89 (sd=8)	92 (sd=23)
Test condition	: The exposure systems used modified proportional diluters with a 0.5 dilution factor. Materials containing plasticizers were not used in the test systems and no cosolvents were used to prepare stock exposure solutions. A stock exposure solution was prepared daily by mixing vigorously and pumping the solutions to the diluter. The stock solution was prepared at the highest concentration tested, which is well below its maximum water solubility.		
	<p>The dilution water used for the study and culturing was well water fortified with salts to increase the hardness to 150 to 180 mg/L as CaCO₃. Alkalinity ranged from 100 to 130 mg/L CaCO₃, pH ranged from 7.9 to 8.3, and temperature was 21 +/- 2 deg C. Dissolved oxygen concentration was greater than 60% saturation and specific conductance was 400 to 600 umho/cm.</p> <p>Five exposure concentrations were used in the study as follows with standard deviation in parenthesis: 130 (21); 59 (6); 25 (3); 16 (2); and 5.8 (1.4)</p> <p>Survival and reproduction were assessed every weekday from day 7 to day 21. Offspring were counted and removed on sampling days. Food was added to test vessels three times a day on weekdays and 2 times a day on weekends and holidays.</p> <p>Dissolved oxygen and temperature were monitored every weekday within one replicate test chamber of each treatment level and control. Total hardness, alkalinity, specific conductance, and pH of test solutions were monitored weekly in one test vessel from each treatment and control.</p> <p>The diluters delivered 50 ml of test solution to each chamber at a rate equivalent to 4.4 to 5.0 volume replacements daily. Illumination to the test systems was provided by Durotest fluorescent lights located above the test chambers. Sixteen hours of light were provided each day at an intensity of 2 to 4 hectolux (2.94 to 5.88 W m⁻²) at the solution surface.</p> <p>Test solutions and control water were analyzed for phthalate ester concentration on day 0, 7, 14, and 21. Two of four replicate test chambers were analyzed on sampling days. On each sampling date, two quality assurance samples were prepared and remained with the set of samples through the extraction and analysis procedures.</p> <p>Each sample was extracted three time with separate 50 ml aliquots of hexane for 2 to 3 minutes. Extracts were combined and volume reduced. Concentrates were stored in 10 ml serum vials at 0 deg C until analyzed. Analysis was by gas chromatography with an electron-capture detector.</p>		
Test substance	: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester		
Conclusion	: Diethyl phthalate produces chronic aquatic toxicity to invertebrates at a concentration below its maximum water solubility.		
Reliability	: (2) valid with restrictions This study is rated a "2" because it used appropriate testing procedures. Although a standard test guideline was not used, the procedure was consistent with currently accepted guidelines. The study procedure and results were accepted in a peer reviewed journal. Additionally, the data are consistent with known toxicological properties of similar low molecular weight phthalate ester substances.		

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4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

Type : LC50
Value : > 4.64 mg/l
Species : rat
Strain :
Sex : no data
Number of animals : 3
Vehicle : other: Undiluted test material administered
Doses :
Exposure time : 6 hour(s)
Method : other
Year : 1968
GLP : no
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Remark : There were no death in any animal tested. The ears, nose and paws were red (day post-exposure not specified). All animals gained weight.

Test condition : Three rats were exposed for 6 hours to a nominal concentration of 4.64 mg/L of the test substance in a whole-body inhalation chamber. The test substance was heated to 150°C to generate the test atmosphere which was likely a mixture of aerosol and heated vapor. The animals were observed for a period of 14 days for survival.

Test substance : 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate)
CAS # 84-66-2

Conclusion : Under the conditions of this study, diethyl phthalate has a low order of acute inhalation toxicity in rats

Reliability : (2) valid with restrictions
Screening study; insufficient number of animals. No analytical chamber concentrations or individual animal observations.

Flag : Critical study for SIDS endpoint
05.07.2006 (4)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 20 ml/kg bw
Species : guinea pig
Strain :
Sex : no data
Number of animals : 1
Vehicle : other: Undiluted test material administered
Doses :
Method : other
Year : 1968
GLP : no
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Result : No animals died. Minimal irritation was observed but not scored. There were no remarkable clinical signs noted during the post-treatment

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Test condition : observation period.
: Three guinea pigs were shaved and depilated prior to dosing. Dose levels of 5, 10, or 20 ml/kg of the neat test substance were applied to the skin (one animal per dose level) and the area wrapped with an impervious material for 24 hours. Following unwrapping, the skin was evaluated for signs of irritation. The animals were observed for a period of 14 days for survival.

Test substance : 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate)
CAS # 84-66-2

Conclusion : Under the conditions of this study, diethyl phthalate has a low order of acute dermal toxicity in rats.

Reliability : (2) valid with restrictions
Screening study; insufficient number of animals.

Flag : Critical study for SIDS endpoint
05.07.2006

(3)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type :
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 16 weeks
Frequency of treatm. : Daily for 16 weeks
Post exposure period : Not applicable
Doses : 0 (control), 0.2, 1.0 or 5.0%
Control group : yes, concurrent no treatment
NOAEL : = 150 - 750 mg/kg
Method : other: No data
Year : 1978
GLP : no data
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Statistics: Mean values compared to controls by Student's t-test and ranking method of Wilcoxon.

Remark : Short term feeding study: There was a statistically significant decrease in body weights of males and females at 5% and in females only at 1% DEP. Similarly, mean food consumption was decreased in males and females at the high dose and in females at the mid dose. Erythrocyte count was higher in males in the 5% DEP group for 6 weeks compared to controls. This increase was followed by hemoglobin levels that were higher than controls. No significant increases in urinary cell excretion were observed in males or females. The relative weights of the brain, liver, stomach and small intestine were higher in males and females at the high dose compared to controls. The only gross abnormality found during autopsy was a

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Result	: unilaterally small testis in one rat which received DEP (0.2%) in the diet.
Test condition	: NOAEL: males (1% ~ 750 mg/kg/day); females (0.2 %, ~ 150 mg/kg/day).
	: Short term feeding study: Groups of 15 males and females were administered diets containing the doses specified above for 16 weeks. Body weight, food and water intake were measured weekly. At the end of the feeding period, rats were fasted overnight and killed by exsanguination from the aorta. Sections of the following organs were removed and preserved in 10% buffered formalin: brain, pituitary, thyroid, heart, liver, kidney, adrenal glands, spleen, gonads, stomach, small intestine, salivary glands, trachea, lung, thymus, urinary bladder, colon, rectum pancreas, uterus, seminal vesicles, and skeletal muscle. Clinical analyses were performed on blood and urine collected at the post-mortem examination.
Test substance	: Paired-feeding study: Groups of six rats of each sex were fed diets containing either control or 5% DEP for 112 days. Each control was from the same litter as one of the treated rats of the same sex. Food consumption and body weight were recorded daily. Each control rat was given an amount of food equal to that consumed in the previous 24-hour period by its paired littermate. Body weights were measured weekly.
Conclusion	: 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate) CAS # 84-66-2
Reliability	: Limited signs of toxicity were observed in male and female rats administered DEP in the diet for periods up to 16 weeks.
Flag	: (1) valid without restriction
03.04.2006	: Critical study for SIDS endpoint

(1)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	: Ames test
System of testing	: Salmonella typhimurium /TA98; TA100; TA1535; TA1537
Test concentration	: 5 Dose levels up to 10 mg/plate
Cycotoxic concentr.	:
Metabolic activation	: with and without
Result	: negative
Method	: OECD Guide-line 471
Year	: 1985
GLP	: no data
Test substance	: other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method	: Statistical Methods: A mutagenic response was defined as a reproducible, dose-related increase in the number of histidine-independent colonies over the spontaneous incidence. There was no requirement for a specific magnitude of increase.
Result	: The test substance was negative in all strains.
Test condition	: Approximately 10E8 bacteria were mixed with 0.5 ml of either 0.1M sodium phosphate buffer or S-9 mix, and test substance. The reaction was carried out in triplicate. The mixture was incubated at 37°C for 48 hours, after which time histidine-revertant colonies were counted. The doses selected were separated by half-log intervals. The high dose was 10 mg/plate unless limited by solubility. Positive control chemicals were sodium azide, nitro-o-phenylenediamine, 9-aminoacridine and 2-aminoanthracene. Concurrent solvent and positive controls were included in all experiments. A toxicity pretest with TA 100 was conducted to determine the high dose level.
Test substance	: 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate) CAS# 84-66-2
Conclusion	: No mutagenic activity was observed at doses up to 10 mg/plate in Salmonella strains TA98, TA100, TA1535 and TA1537 with or without

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Reliability	: metabolic activation. (1) valid without restriction NTP-sponsored study.	
Flag 05.07.2006	: Critical study for SIDS endpoint	(18)
Type	: Chromosomal aberration test	
System of testing	: Non-bacterial: Chinese hamster ovary cells	
Test concentration	: 12.5 hr incubation: 70, 151, and 324 mg/ml 15.5 hr incubation: 70, 151, and 324 mg/ml	
Cycotoxic concentr.	:	
Metabolic activation	: with and without	
Result	: negative	
Method	: OECD Guide-line 473	
Year	: 1987	
GLP	: yes	
Test substance	: other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester	
Method	: Statistical tests were performed on both the dose response curve and individual dose points. A statistically significant ($P < 0.05$) difference for one dose point and a significant trend ($P < 0.015$) were considered weak evidence of a positive response; significant differences for two or more doses indicate the trial is positive.	
Result	: Metabolic Activation: With and without S9 (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rats). Negative. A small dose-related increase in the percentage of aberrations was observed in one trial without S9; however, this finding was insufficient to be considered positive because no single dose was significantly elevated above the control.	
Test condition	: In the assay without S9, cells were incubated in McCoys 5A medium for 8.5 hours. Colcemid was added and incubation continued for 2 hours. Cells treated with S9 were treated with diethyl phthalate for 2 hours, after which the treatment medium was removed and cells were then incubated for 10 hours in fresh medium. Colcemid was added during the final 2 hours of the incubation. Cells were selected for scoring based on good morphology and karyotype. Slides were scored blind and were read by the same person. DMSO was used as the solvent control at both incubation time points. Mitomycin-C was used as the positive control at 15.5 hours and cyclophosphamide served as the positive control for the 12.5 hour time point.	
Test substance	: 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate) CAS # 84-66-2	
Conclusion	: Under conditions of this study, diethyl phthalate was inactive in the chromosome aberration assay.	
Reliability	: (1) valid without restriction	
Flag 05.07.2006	: Critical study for SIDS endpoint	(10)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	: Two generation study
Species	: mouse

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Sex	: male/female
Strain	: other: Swiss CD-1
Route of admin.	: oral feed
Exposure period	: Continuous throughout study (beginning 7 days prior to mating).
Frequency of treatm.	: Daily throughout premating, mating, gestation, and lactation
Premating exposure period	
Male	: 7 days
Female	: 7 days
Duration of test	: 2 generations
No. of generation studies	:
Doses	: 0.0, 0.25, 1.25, or 2.5% (~0, 325, 1625, or 3250 mg/kg).
Control group	: yes, concurrent no treatment
NOAEL parental	: 3250 mg/kg bw
NOAEL F1 offspring	: 3250 mg/kg bw
NOAEL F2 offspring	: 3250 mg/kg bw
Method	: other: continuous breeding study
Year	: 1987
GLP	: no data
Test substance	: other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester
Method	: Statistical methods: Cochran-Armitage (dose-related trends); Fisher's exact test (mating and fertility trends); Kruskal-Wallis test and Jonckheere's test (group means for sex ratio); Wilcoxon-Mann-Whitney U test (pairwise comparisons of treatment group means).
Result	: NOAEL: 2.5% for fertility and reproductive endpoints. DEP had no effect on the numbers of fertile pairs, the number of litters per pair, the number of pups per litter, live pup birth weight or the proportion of pups born alive. In the F1 generation, comparisons were made between 0.0 (control) and 2.5% (high dose) animals only. DEP had no effect on fertility, proportion of live births, pup weight or sex. The number of live pups per litter was decreased, however at 2.5%. In addition, statistically significant decreases in body weight were observed in males and females. There were increases male prostate and female liver weight and a decrease in female pituitary weight. DEP had no effect on sperm motility; however, sperm concentration decreased in the treated animals.
Test condition	: There were 40 animals/sex in the untreated control group. Males and females in the treatment groups (20 animals/sex) were exposed to the test substance beginning with a 7-day premating period and throughout a cohabitation period for approximately 14 weeks. Reproductive function was assessed during this cohabitation period for number of litters per pair, number of live pups, sex, live births, and pup weight. These litters were subsequently discarded. Following the 14-week cohabitation, the pairs were separated during which any final litters were delivered and kept for assessment of the next generation fertility (F1). When the F1 litters were sexually mature, they were mated with animals from different litters within the same group. The F2 litters were examined for litter size, survival, sex and pup weight. The F1 animals were then necropsied. F0 parameters evaluated: clinical signs, mortality, body weight gain, consumption of food and water. F1 parameters evaluated: reproductive performance, litter size, survival, sex and pup weight F2 parameters evaluated: litter size, survival, sex and pup weight. Sperm examination: Epididymis from the right cauda was excised. The percentage of motile sperm under 400 magnification was determined. Necropsies: In females, endpoints examined included organ weights and histology. In males, organ weights, histology, percentage of, motile sperm, sperm concentration and percentage of abnormal sperm was assessed. Clinical observations were performed on blood and urine collected at the post-mortem examination.
Test substance	: 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate) CAS#: 84-66-2
Conclusion	: DEP caused decreased body weight gain at 2.5%, but did not affect

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Reliability : reproduction. The data from this study confirmed that DEP is not a reproductive toxicant.
: (2) valid with restrictions
Flag : Only high dose tested in F1 generation.
05.07.2006 : Critical study for SIDS endpoint

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5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : Gestation day 6-15
Frequency of treatm. :
Duration of test :
Doses : 0.0, 0.25, 2.5 or 5.0%
Control group : yes
NOAEL maternal tox. : = 200 mg/kg bw
NOAEL teratogen. : = 1910 - mg/kg bw
Method : OECD Guide-line 414 "Teratogenicity"
Year : 1993
GLP : yes
Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Statistical methods: ANOVA; Williams' and Dunnett's Multiple Comparison Test, Fisher's exact probability test.

Result : NOAEL for maternal toxicity: 0.25% (0.20 g/kg/day).
NOAEL for developmental toxicity: 2.5% (1.91 g/kg/day).
LOAEL for developmental toxicity: 5.0% (3.21 g/kg/day).

Maternal effects: Actual doses received: 0.20, 1.91 and 3.21 g/kg/day based on body weights and food consumption. No dams died during gestation. Food consumption and body weight decreases were observed for the 2.5% and 5.0% treatment groups. Food consumption decreased by 20% and 52% in the 2.5% and 5.0% treatment groups, respectively. Body weight gain during treatment was suppressed in the 5.0% dosing group. Reductions in absolute weight gain and corrected gestational weight gain were observed in the 5.0% dosing group. The effect at 2.5% was transient and considered related to the unpalatability of the test feed mix. No effects on kidney or liver weight were observed.

Embryo/fetal effects: No significant findings for number of resorptions, number of implantations, pre- and post-implantation loss or number of corpora lutea. No effects on viability, litter size or mean fetal body weight. No increases in the incidence of fetuses malformed per litter or the percentage of litters with malformations were observed. A statistically significant increased incidence of fetuses exhibiting skeletal variations (particularly supernumerary ribs) was observed at 5.0%, however there was also a high incidence of skeletal variations in the control group. This skeletal variation is generally considered a secondary effect of maternal toxicity and stress, therefore its significance is unclear.

Test condition : After a 7 day quarantine period, breeding pairs were cohabited overnight. Gestation day 0 was determined the morning that vaginal sperm was found. Initial body weights of females were between 207-273 grams. On gestation day 0, animals were randomly assigned to treatment groups consisting of 25-32 animals. Animals were weighed on the morning of gestation day 0, 3, 6, 9, 12, 15, 18 and 20. In addition, animals were observed daily for signs of toxicity. Maternal body, liver, kidneys, and intact uterus were weighed. Fetuses were weighed, examined for external

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Test substance : abnormalities and received a visceral examination.
: 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate)
CAS # 84-66-2. Purity of the test substance was >99%.

Conclusion : Under the conditions of this study, DEP was not a selective developmental toxicant. DEP exposure was associated with maternal effects and an increased incidence in fetal supernumerary ribs at the highest dose tested (5.0%).

Reliability : (1) valid without restriction
Guideline study.

Flag : Critical study for SIDS endpoint
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5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type : other: Two generation study

In vitro/in vivo :

Species : mouse

Sex : male/female

Strain : other: Swiss CD-1

Route of admin. : oral feed

Exposure period : Continuous throughout study (beginning 7 days prior to mating).

Frequency of treatm. : Daily throughout premating, mating, gestation, and lactation

Duration of test : 2 generations

Doses : 0.0, 0.25, 1.25, or 2.5% (~0, 325, 1625, or 3250 mg/kg).

Control group : yes, concurrent no treatment

Method : other: continuous breeding study

Year : 1987

GLP : no data

Test substance : other TS: CAS #84-66-2; 1,2-Benzenedicarboxylic acid, diethyl ester

Method : Statistical methods: Cochran-Armitage (dose-related trends); Fisher's exact test (mating and fertility trends); Kruskal-Wallis test and Jonckheere's test (group means for sex ratio); Wilcoxon-Mann-Whitney U test (pairwise comparisons of treatment group means).

Remark : Premating exposure period: males 7 days; females 7 days

Result : NOAEL Parental 3250 mg/kg bw
NOAEL F1 Offspr. 3250 mg/kg bw
LOAEL F1 Parental 1625 mg/kg bw
NOAEL F2 Offspr. 3250 mg/kg bw
: NOAEL: 2.5% for fertility and reproductive endpoints.

DEP had no effect on the numbers of fertile pairs, the number of litters per pair, the number of pups per litter, live pup birth weight or the proportion of pups born alive. In the F1 generation, comparisons were made between 0.0 (control) and 2.5% (high dose) animals only. DEP had no effect on fertility, proportion of live births, pup weight or sex. The number of live pups per litter was decreased, however at 2.5%. In addition, statistically significant decreases in body weight were observed in males (12%) and females (8%). There was a 32% increase in male prostate and a 15% increase in female liver weight. In addition there was a 17% decrease in female pituitary weight. DEP had no effect on sperm motility; however, sperm concentration decreased in the treated animals.

Test condition : There were 40 animals/sex in the untreated control group. Males and females in the treatment groups (20 animals/sex) were exposed to the test substance beginning with a 7-day premating period and throughout a cohabitation period for approximately 14 weeks. Reproductive function was assessed during this cohabitation period for number of litters per pair, number of live pups, sex, live births, and pup weight. These litters were subsequently discarded. Following the 14-week cohabitation, the pairs

were separated during which any final litters were delivered and kept for assessment of the next generation fertility (F1). When the F1 litters were sexually mature, they were mated with animals from different litters within the same group. The F2 litters were examined for litter size, survival, sex and pup weight. The F1 animals were then necropsied. F0 parameters evaluated: clinical signs, mortality, body weight gain, consumption of food and water. F1 parameters evaluated: reproductive performance, litter size, survival, sex and pup weight F2 parameters evaluated: litter size, survival, sex and pup weight. Sperm examination: Epididymis from the right cauda was excised. The percentage of motile sperm under 400 magnification was determined. Necropsies: In females, endpoints examined included organ weights and histology. In males, organ weights, histology, percentage of motile sperm, sperm concentration and percentage of abnormal sperm was assessed. Clinical observations were performed on blood and urine collected at the post-mortem examination.

Test substance : 1,2-benzenedicarboxylic acid, diethyl ester (diethyl phthalate)
CAS#: 84-66-2

Conclusion : DEP caused decreased body weight gain at 2.5%, but did not affect reproduction. The data from this study confirmed that DEP does not affect reproductive performance.

Reliability : (2) valid with restrictions
Only high dose tested in F1 generation.

Flag : Critical study for SIDS endpoint
14.04.2006 (8)

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

- (1) Brown D, Butterworth KR, Gaunt IF, Grassom P and Gangolli SD (1978). Short-term oral toxicity study of diethyl phthalate in the rat. *Food and Cosmetic Toxicology* 16, 415-422.
- (2) Cousins I and Mackay D (2000). Correlating the physical-chemical properties of phthalate esters using the 'three solubility' approach. *Chemosphere* 41, 1389-1399.
- (3) Eastman Kodak Company (1968). Diethyl Phthalate. Acute Dermal Toxicity. Unpublished report.
- (4) Eastman Kodak Company (1968). Diethyl Phthalate. Acute Inhalation Toxicity. Unpublished report.
- (5) EG&G Bionomics, Inc. (1983). Acute Toxicity of Fourteen Esters to Rainbow Trout *Salmo gairdneri* Under Flow-Through Conditions. Report No. BW-83-3-1373. Unpublished report.
- (6) Environmental Protection Agency (EPA) (2000). EPI SuiteTM, Estimation Program Interface Suite, v3.12. U.S. EPA, Washington, DC, USA.
- (7) Field, et al (1993). Developmental toxicity evaluation of diethyl and dimethyl phthalate in rats. *Teratology* 48, 33-44.
- (8) Lamb IV JC, Chapin RE, Teague CJ, Lawton AD and Reel JR (1987). Reproductive effects of four phthalate acid esters in the mouse. *Toxicology and Applied Pharmacology* 88, 255-269.
- (9) Mackay D (1998). Level III Fugacity-Based Environmental Equilibrium Partitioning Model, Version 2.1 (16-bit). Environmental Modelling Centre, Trent University, Ontario, Canada.
- (10) National Toxicology Program (NTP) (1995). Toxicology and Carcinogenesis Studies of Diethylphthalate in F344/N Rats and B6C3F1 Mice with Dermal Initiation/promotion Study of Diethylphthalate and Dimethylphthalate in Male Swiss CD-1 Mice. NTP TR 429, NIH Publication No. 95-3356.
- (11) Rhodes J, Adams W, Biddinger G, Robillard K and Gorsuch J (1995). Chronic toxicity of 14 phthalate esters to *Daphnia magna* and Rainbow trout (*Oncorhynchus mykiss*). *Environ Toxicol Chem* 14, 1967-1976.
- (12) Springborn Bionomics, Inc. (1984). Acute Toxicity of Fourteen Esters to *Daphnia magna*. Report No. BW-84-4-1567. Unpublished report.
- (13) Springborn Bionomics, Inc. (1984). Acute Toxicity of Fourteen Esters to the Freshwater Green Alga *Selenastrum capricornutum*. Report No. BP-84-1-4. Unpublished report.
- (14) Staples C, Peterson D, Parkerton T and Adams W (1997). The environmental fate of phthalate esters: A literature review. *Chemosphere* 35, 667-749.
- (15) Staples CA, et al (1997). Aquatic toxicity of eighteen phthalate esters. *Environmental Toxicology and Chemistry* 16(5), 875-891.
- (16) Sugatt R, et al. (1983). Shake Flask Biodegradation of 14 Commercial Phthalate Esters. Syracuse Research Corporation, Syracuse, NY, USA. SRC# L1543-05.
- (17) Sugatt R, O'Grady D, Banerjee S, Howard P and Gledhill W (1984). Shake flask biodegradation of 14 commercial phthalate esters. *App Environ Microbiol* 47, 601-606.
- (18) Zeiger E, Haworth S, Mortelmans K and Speck W (1985). Mutagenicity testing of Di(2-ethylhexyl) phthalate and related chemicals in salmonella. *Environmental Mutagenesis* 7, 213-232.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

Memo : This chemical is part of the Low Molecular Weight Phthalate Esters subcategory. Data from other chemicals in this subcategory can be used to assess the potential hazards of all category members.

Remark : There is a large amount of data for the physicochemical properties of dimethyl and diethyl phthalate. Computer models were also used to estimate these properties for comparison with measured values and additionally were used to predict environmental distribution.

A complete health effects SIDS data set is available for diethyl phthalate, and for dimethyl phthalate with the exception of adequate reproductive data. Both DMP and DEP show minimal acute toxicity, are not genotoxic, exhibit some liver and kidney effects at high doses, and are negative for developmental effects. Although adequate reproductive data are not available for DMP, data on DEP indicate that this material will not cause reproductive effects. This is further supported by data showing that neither DEP nor DMP had effects on male reproductive development. The lack of developmental effects observed with DMP, coupled with chronic toxicity studies showing no effects on reproductive organs, negates the need to conduct a reproductive study for DMP.

There are numerous published acute aquatic toxicity studies in a variety of species of fish, daphnia and algae for DMP and DEP. DMP and DEP are slightly soluble in aqueous systems. Acute effects on aquatic species are seen in the 10 to 100 ppm range.
Chapters 2,3,4 & 5

02.11.2001

10.3 RISK ASSESSMENT